Adv Physiol Educ 39: 383–391, 2015;
doi:10.1152/advan.00045.2015.

A multidisciplinary guided practical on type I diabetes engaging students in inquiry-based learning

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Submitted 18 March 2015; accepted in final form 13 October 2015

Mingueneau M, Chaix A, Scotti N, Chaix J, Reynders A, Hammond C, Thimonier J. A multidisciplinary guided practical on type I diabetes engaging students in inquiry-based learning. *Adv Physiol Educ* 39: 383–391, 2015; doi:10.1152/advan.00045.2015.—In the present article, we describe a 3-day experimental workshop on type I diabetes aimed at helping high school students to understand how fundamental research on glycemia regulation contributes to the development of scientific knowledge and therapeutic strategies. The workshop engaged students in open-ended investigations and guided experiments. Each class was divided into three or four groups, with each group working with a trained doctoral student or postdoctoral fellow. During an initial questioning phase, students observed slides depicting the glycemia of individuals in various situations. Students identified hyperglycemic individuals relative to the average glycemia of the displayed population. Students were asked to devise a treatment for these diabetics. They quickly realized that they couldn't experiment on patients and understood the need for laboratory models. Each group gave ideas of experiments to perform. We then explained, taking into account their propositions, the protocols students could execute to address one of the following questions: Which criteria must an animal model of diabetes fulfill? How do pancreatic cells maintain glycemia? Is there a way to produce an insulin protein similar to the one released by human pancreatic cells? We used two different evaluation metrics of the workshop: a questionnaire filled out by the students before and after the workshop and a poster produced by students at the end of the workshop. We found that this educational approach successfully improved student awareness and understanding of the scientific reasoning and research process.

inquiry-based learning; blood glucose physiology; diabetes; high school students; undergraduate students

THE WORKSHOP PRESENTED in the present article engaged students in open-ended investigations and guided experiments (8). The principle of this active inquiry-based learning technique initially proposed almost 50 yr ago (2) is that knowledge is built from an initial question rather than from statements and is enhanced in a step-wise fashion by ideas of experiments proposed by students themselves rather than transferred passively from the teacher to the students in one single step (4, 6, 9, 17). Although open-ended and guided investigation methods have proven to be effective and highly motivational instructional strategies (10), designing such practicals remains challenging because of the logistic and conceptual hurdles associated with this type of pedagogy.

The workshop aimed at helping students understand how the scientific results they study in their biology courses originate in research laboratories and how glycemia (blood glucose levels) is regulated. These topics were taught via hands-on experiments and in a multidisciplinary context that helped students understand the link between fundamental research and therapeutic innovations. During an initial questioning phase, students observed PowerPoint slides depicting the glycemia of individuals in various situations. They suggested to identify hyperglycemic individuals relative to the average glycemia of the displayed population. Students were asked to devise a treatment for these diabetics in the absence of research on the subject in the literature. They quickly realized that they couldn't experiment on patients and understood the need for laboratory models. The present workshop allowed students to explore some of the steps researchers had to take before designing treatments for type I diabetes. During this process, students thought about the following questions (these questions were never directly asked to the students; tutors used these questions to guide the discussion, if necessary; Fig. 1):

- Which criteria must an animal model of diabetes fulfill? Students thought about the need for cellular and animal models to understand pancreatic physiology and dysfunction in the course of the disease. They identified the criteria that an animal model of type I diabetes must fulfill (high glycemia, poor glycemia regulation, typical histology of the endocrine pancreas, and lack of insulin in pancreatic β-cells) and determined whether the model that we provided met these criteria.
- How do pancreatic cells maintain glycemia? Based on the analysis of the PowerPoint slides we provided, students often suggested that a molecule synthesized by pancreatic cells might regulate glycemia. To identify the molecular nature of insulin, we asked students to cite molecules they knew. They often cited DNA and proteins. They usually reasoned that DNA was not a good candidate since it is not secreted by cells. We next encouraged them to think about the mechanisms by which insulin could ensure the maintenance of glucose homeostasis and by which mechanisms pancreatic cells could sense variations in glycemia and trigger insulin secretion to maintain glycemia. Insulin receptors and intracellular pathways were not studied during the workshop.

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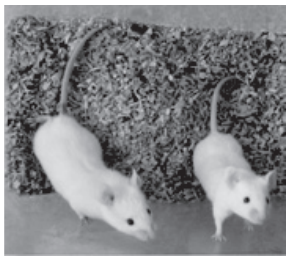

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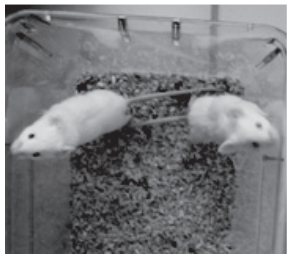

Diabetic?

Group 1

Which criteria must an animal model fulfill?

- Observation of the behavior of control and alloxan-treated mice
- Measurements of glycemia and glycosuria
- Dissection of the mouse, study of pancreas slices
- Effect of alloxan on a pancreatic β cell line

Group 2

How do pancreatic cells maintain glycemia while the entry of glucose in the organism is highly variable?

- Stimulation of INS1-E cells
- Quantification of insulin secretion as a function of glucose concentration

Group 3

How to engineer a genetically modified organism that would produce a functional insulin protein similar to the one released by mammalian pancreatic β cells?

- Transfection of CHO cells with plasmid DNA coding for insulin and GFP
- Boinformatics

All Groups

How to test the efficacy of the insulin produced?

- Design of the protocol

Fig. 1. Summary of the practical with the different questions tested and experiments conducted by the students to answer them (for tutors only). INS1-E cells are an insulin-secreting cell line derived from β-pancreatic cells. CHO cells are a cell line derived from Chinese hamster ovary cells, which were used here for the production of insulin. GFP, green fluorescent protein. The ELISA test is a test that uses antibodies to quantify various molecules (here, insulin).

- Is there a way to produce an insulin protein similar to the one released by human pancreatic cells? Students applied the knowledge generated above to design a method to produce large quantities of human insulin: since it is a protein, the gene coding for it can be introduced into a microorganism or a cell line to engineer a genetically modified organism, but will this insulin be similar to the insulin produced by pancreatic β-cells? What methods could be used to determine whether this recombinant insulin will work in mammals?

During this inquiry-based workshop, each group provided ideas of experiments to perform. Taking into account their propositions, we then discussed the question they could focus on and the experimental strategies they could take to address it (Fig. 1). At the end of the experimental session, students made posters and presented their work to researchers. The workshop was designed to promote exploration, stimulate creativity, and generate enthusiasm about a topic that can be relatively abstract and poorly motivating for students when taught in a traditional learning context.

METHODS

Workshops took place in a research laboratory for high school students in a research institute of the French Medical Research Council [Institut National de la Santé et de la Recherche Médicale (INSERM)] on a scientific campus of Aix-Marseille University in France. The laboratory is managed by the nonprofit organization Tous Chercheurs, loosely translated as "We're All Researchers," reflecting its philosophy that everyone can be a researcher for at least a little while. The program for high school students is now 10 yr old. Tous Chercheurs School has from its inception complied with the rules of INSERM. In particular, high school students used names of their choice with no personal information that might allow identification of individuals. Human subject approval was not needed for this study since questionnaires were anonymous. Workshops lasted 3 full days, took place during school time, and were free of charge; high schools only paid for transport to the laboratory. All students in a volunteer class participated in the workshop. Mice were maintained in specific pathogen-free conditions and were handled in accordance with French and European directives (Animal Protocol Agreement D1305519 of the INSERM Animal Care and Use Committee).

Groups of Students and Tutors

Students who attended the workshop were not required to have previous experience with laboratory practice. Classes were divided into three (for classes of up to 24 students) or four (for classes of 25–32 students) groups of six to eight students by the teacher before the workshop. Each group was tutored by a doctoral student or a postdoctoral fellow (1 tutor for 6–8 students, i.e., 3–4 tutors/class). These tutors were mainly volunteers working in the laboratories of Aix-Marseille University. They received individual training in inquiry-based learning and experimental protocols on diabetes from the Tous Chercheurs team before their participation in workshops. During this training, we first presented the objectives and pedagogy of Tous Chercheurs. We also introduced the concepts of inquiry-based learning and open-ended investigations. We then played the role of the tutor, and the future tutor took the place of a student while observing the slides of the first morning. We also discussed the following topics: how the tutor must behave toward students, health and safety recommendations, the subject of the workshop, and the experiments tutors would have to perform. After the training, the future tutors had to learn more about the subject of the workshop by themselves. They were paid for their participation in the workshop.

Schedule of the Workshop

The schedule of the workshop is shown in Fig. 2.

Phase 1 of the workshop: open-ended questioning (day 1). The session began with a period of 3 h, during which students had to think about glycemia homeostasis and regulation in the mammalian body. We provided them with illustrated data (PowerPoint slides) displaying blood glucose concentrations in various situations (Fig. 3, *A*, *C*, and *D*). Students asked questions and their tutor made sure they carefully observed the results shown in the slides. Students first observed the distribution of glycemia of 120 human fasting subjects (Fig. 3*A*). Students quickly noticed that most individuals had a glycemia value close to 1 g/l. They also identified individuals with extreme values among the tested population: 0.70 and 2.05 g/l. As the majority of individuals had glycemia close to 1 g/l, students hypothesized that this was the mean control value. At that point, tutors asked them to more precisely calculate this mean value [mean (±SE) glycemia: 0.97 ± 0.29 g/l, $n = 120$] as well as the fraction of individuals with glycemia

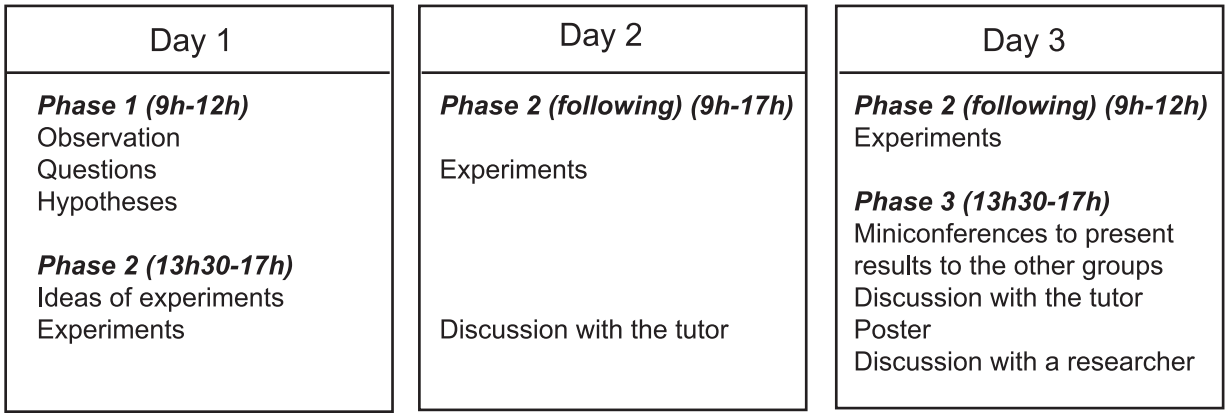

Fig. 2. Schedule of the workshop.

values below and above 1 g/l. Students were asked to graphically represent these calculations. Two examples of plots produced by the students are shown in Fig. 3*B*. Most of the students produced the graphical representation of Fig. 3*B*, *top*, and observed that there were more individuals with a glycemia of ≤1 g/l than there were with hyperglycemia (>1 g/l). They then decided to calculate the mean glycemia for these two populations. The mean glycemia for the "control" population was 0.83 ± 0.08 g/l (n = 90), and the mean glycemia for the "hyperglycemic" population was 1.39 ± 0.30 g/l (n = 30). Students who were aware of diabetes stated that some of these hyperglycemic individuals might be diabetic. When we told them that a glycemia value of <0.74 g/l was termed hypoglycemia, some of the students suggested a different graphical representation to more accurately represent the distribution of glycemia values shown in Fig. 3*A* (Fig. 3*B*, *bottom*). Students typically inquired about the symptoms associated with hypoglycemia or hyperglycemia.

Next, students observed the diagram showing the glycemia of a control subject over 24 h (Fig. 3*C*). From that diagram, students reported that half an hour after each meal (8.30 AM, 12.30 PM, and 5.30 PM), glycemia slightly increased and within 2–3 h went back to its preprandial value. The increase of glycemia varied with the type of meal. Students also observed that glycemia typically stabilized at a value close to 5 mmol/l. They often asked about the mechanisms by which glycemia was maintained between meals. We asked them to compare the results of Fig. 3, *A* and *C*. To do so, they had to convert molar concentrations (mmol/l) to mass concentrations (g/l).

Finally, students analyzed the impact of pancreatectomy on the glycemia of a dog and the effect of a pancreatic graft on the glycemia of the same pancreatectomized dog (Fig. 3*D*). Students observed that after removal of the pancreas, glycemia jumped to 3–4 g/l. They concluded that the pancreas likely played a key role in the regulation of glycemia. To test this hypothesis, they proposed a pancreas transplant. Students observed that after pancreas transplant, glycemia progressively decreased over a 6- to 7-h period and stabilized to a value centered around 1 g/l. If the graft was then removed, glycemia increased again. They asked questions such as "How does the pancreas regulate glycemia?" and "Do diabetic individuals lack a pancreas or is their pancreas nonfunctional?" When they did not know that insulin is released by pancreatic cells and plays a role in glycemia regulation, we told them how insulin was discovered and that this secreted molecule has a key function in the pancreatic regulation of glycemia. We then asked them how they would proceed to understand the physiology of pancreatic cells, how pancreatic cells regulate glycemia thanks to insulin, and which part of this function is affected in diabetic patients.

Phase 2 of the workshop: generation of hypotheses and experimental strategies (day 1). Students were then asked how they would proceed to treat individuals they previously identified as diabetic. The goal was to drive students to think about different ways of treating diabetes as well as to get them to realize how crucial a good understanding of fundamental physiology is to generate an adequate therapeutic strategy. This exercise included the design of models (cellular and animal models) to study pancreatic physiology and to test therapeutic strategies. We also asked them how they would like to test their hypotheses empirically. Tutors addressed questions that were raised by students and reframed discussions, but they were instructed not to add or teach additional information not initiated by students.

During this phase of the workshop, students asked questions and proposed ideas using their knowledge of basic biology, their observation skills, and their own reasoning, analytic skills, and inventiveness. Students could propose any type of reasoning and any ideas of experiments as long as they were logical and deduced from their observations. We then explained why their propositions were plausible or not. However, when they needed to know specific points (what is alloxan, what is an ELISA test, or what is spectrophotometry, for example), the tutor gave explanations during the experimental session or students looked for them on the internet. However, during *phases 1* and *2* of the workshop, while they were observing and reasoning, they were not given access to the internet to make sure that they developed independent critical thinking.

At the end of the first morning (after *phases 1* and *2*, see below), tutors explained to the students that research is a collaborative effort and that they would only test one of the questions they thought about while the two or three other groups would work on other complementary questions. The intent of this approach was to demonstrate that scientific knowledge develops through collaboration between independent laboratories on complementary questions. Each group was then assigned an experiment, with their consent. In larger classes, two groups addressed the same experimental question. The corresponding experiments and protocols have been very precisely described in an article recently published in *Advances in Physiology Education* (15).

Phase 3 of the workshop: experimentation, data analysis, and interpretation (days 1–3). Students experimented for 2.5 days, during which they learned to read and follow a protocol, design negative and positive control experiments, manipulate models, quantify results, and discuss and interpret results. In parallel, they made slides summarizing their hypotheses and experimental work. The following three groups of students explored the questions described in the laboratory protocols in Ref. 15 (Fig. 1):

GROUP 1: WHICH CRITERIA MUST AN ANIMAL MODEL OF TYPE 1 DIABETES FULFILL? (7, 13, 16, 19). This group studied mice treated with alloxan, a toxic glucose analog that selectively destroys pancreatic β-cells when administered to rodents.

A

0.70	0.70	0.75	0.80	0.85	0.90	1.15	1.00	1.40	1.10
1.00	0.85	0.85	0.90	0.80	0.90	0.80	1.00	0.80	1.10
0.80	0.70	0.75	1.10	0.80	0.70	0.90	1.20	1.55	0.80
1.00	0.85	0.75	0.80	0.80	0.90	1.95	0.70	1.55	1.20
0.80	1.95	0.75	1.40	0.85	0.80	0.95	0.70	0.80	1.20
1.40	0.85	0.75	0.90	0.75	0.80	0.95	1.00	1.05	1.00
0.80	1.00	0.80	0.90	0.85	0.90	0.95	0.80	1.05	1.00
0.80	1.80	0.80	0.80	0.75	0.75	0.80	0.80	0.85	0.85
0.75	0.80	0.75	0.80	0.75	1.50	0.80	0.80	0.85	0.75
0.75	0.80	1.85	0.80	1.05	0.90	0.80	1.50	0.85	0.75
0.75	0.80	0.95	1.80	1.05	0.85	0.95	1.60	0.85	0.85
1.15	0.80	0.95	1.85	1.05	1.25	1.25	0.90	0.85	0.85

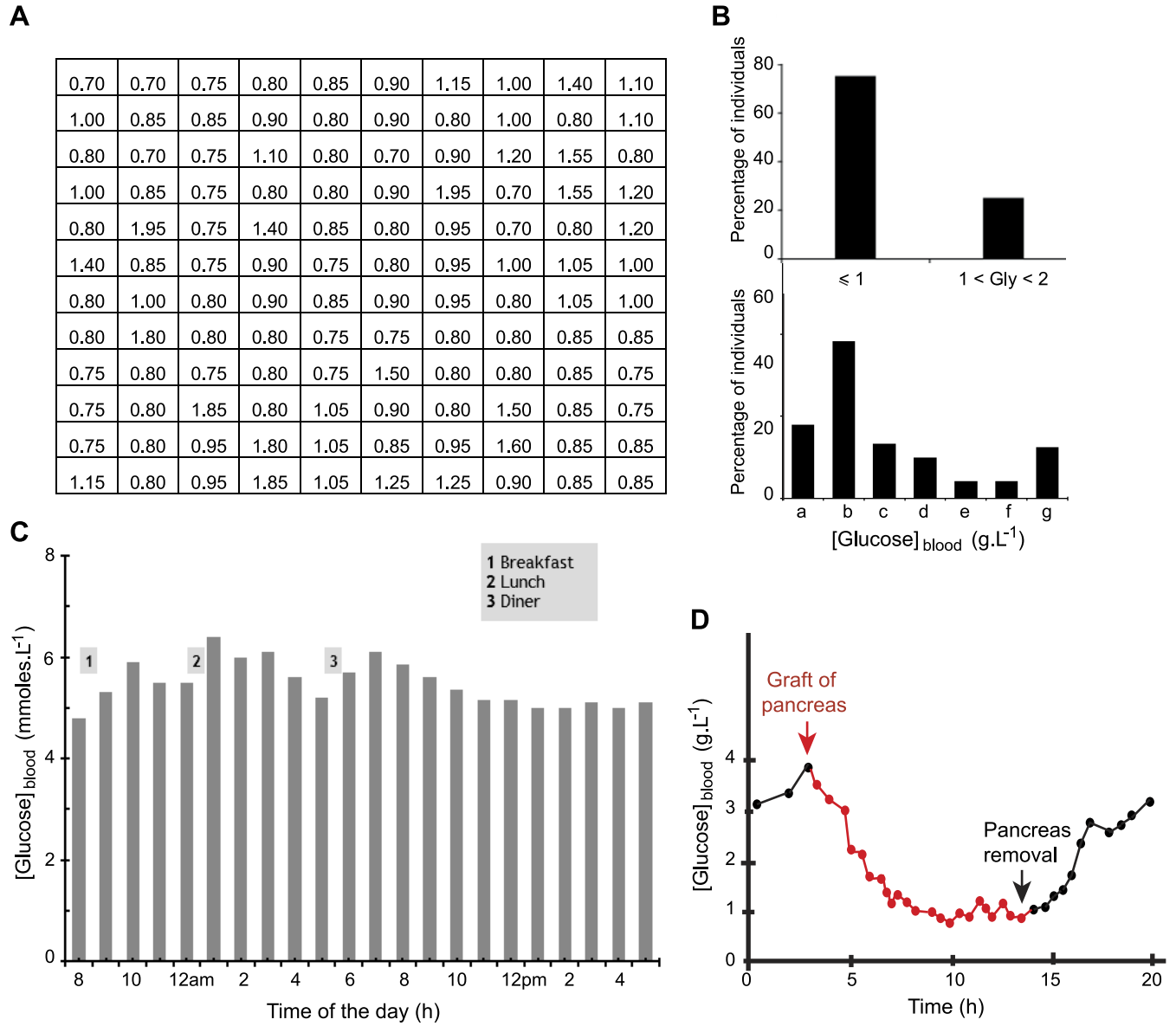

Fig. 3. Data shown to students during the questioning phase. *A*: glycemia values (Gly; blood glucose concentration in g/l) of 120 human fasting subjects. The order of entries has no significance. *B*: two diagrams produced by students from the table shown in *A*. In the bottom diagram, the values of glycemia are 0.70–0.75 g/l in *column a*, 0.80–0.85 g/l in *column b*, 0.90–0.95 g/l in *column c*, 1.00–1.05 g/l in *column d*, 1.10–1.15 g/l in *column e*, 1.20–1.25 g/l in *column f*, and >1.30 g/l in *column g*. *C*: glycemia of a control subject over 24 h. The *x*-axis shows hours (upward ticks) and half hours (downward ticks). *D*: glycemia of a dog after removal of the pancreas (black circles), after pancreatic graft of the pancreatectomized dog (red circles), and again after removal of the pancreas (black circles).

GROUP 2: HOW DO PANCREATIC B-CELLS MAINTAIN GLYCEMIA WHILE GLUCOSE CONSUMPTION AND ABSORPTION IN THE ORGANISM ARE HIGHLY VARIABLE? (3, 14). This group studied insulin production by INS-1 pancreatic cells (a rat pancreatic β-cell line) in response to different doses of glucose.

GROUP 3: IS THERE A WAY TO ENGINEER A GENETICALLY MODIFIED ORGANISM THAT WOULD PRODUCE AN INSULIN PROTEIN SIMILAR TO THE ONE RELEASED BY MAMMALIAN PANCREATIC B-CELLS? (18)? This group studied ways to produce large quantities of human insulin.

Phase 4 of the workshop: communication of the results (day 3). On the afternoon of *day 3*, each group of students explained the question they investigated to the other groups as well as the results obtained and the conclusions drawn, with the aid of the presentation slides they prepared during the workshop. Tutors moderated the session and made sure that the audience asked questions and understood the conclusions reached by each group as well as the links among the work done by each group. Students were then reshuffled into three new groups, "chimera groups" containing students from each of the previous groups. Each chimera group designed a poster summarizing the three questions and experiments. Students from each group explained their poster to an external researcher (from scientific institutes in the area) and discussed the poster with him/her. This oral presentation, which generally lasted ~1 h, ended the session.

Evaluation of Student Work

The efficacy of the workshop was assessed using two different methods: a questionnaire filled out by the students before and after the workshop and a poster produced by the students at the end of the workshop. We evaluated the extent to which students acquired knowl-

Table 1. *Questionnaire given to students before and after the workshop as well as evaluation method and criteria for question 1 ("Describe a researcher's daily job.")*

Example of good answers	Code (meaning)	Score
He/she improves people's lives, finds new drugs or new techniques	Applied research	1
He/she increases knowledge	Fundamental research	1
He/she	Experimental or	1
Observes	investigative	1
Asks questions, finds a problem to solve	approach	1
Creates hypotheses		1
Performs experiments		1
Obtains results, interprets results, and concludes		1
Communicates his/her results		
When the above activities are given in the right order		1

Scores are additive.

edge of how researchers think and conduct their research; acquired experimental and analytic skills; and understood the independent experimental approaches, associated conclusions, and interconnections between fundamental versus applied research strategies. Knowledge on glycemia regulation and diabetes was tested by science teachers during high schools exams to which we were not granted access.

Questionnaire. Students were asked to fill out a questionnaire at the very beginning of the workshop. They were then asked to fill out the same questionnaire at the end of the workshop. Students were not told that the same questions would be asked at the end of the workshop. The questionnaire asked all students the same four questions as follows:

- *Question 1*. Describe a researcher's daily job.
- *Question 2*. What is the difference between an observation and an interpretation? Give an example.
- *Question 3*. What is the difference between a question and a hypothesis? Give an example.
- *Question 4*. How do you make sure that the result obtained from an experiment is a valid result?

To evaluate the questionnaires and to mitigate bias in the analysis, we implemented the following measures: two independent raters (one researcher and one science teacher) who had not attended the corresponding workshop sessions were involved in evaluating all student responses; they were blinded to whether the questionnaires had been filled out before or after the experimental session; qualitative content analysis (12) was applied to *question 1*. The answers given by each individual were evaluated against the expected features of a "good answer" as defined in Tables 1–4. Key elements of a good answer and coding were determined by the raters after having read all the responses but before scoring. The score was *1* for a good answer and *0* for a bad answer. For each student, the relative improvement (or absence of improvement) in the quality of the answer for each question was determined by comparing the scores before and after the workshop using R software (Fig. 4). We first evaluated interrater reliability by comparing the total scores given by each evaluator to each student for the four questions following the assessment grid shown in Tables 1–4 (Fig. 4*A*). Boxplots of the scores given by *rater 1* and *rater 2* for each of the four questions before and after the workshop were then constructed (Fig. 4*B*). We tested whether the probability of getting higher scores with one rater (Fig. 4*A*) or of getting higher scores after compared with before the workshop (Fig. 4*B*) were significant using paired Student's *t*-tests. Finally, the plots shown in Fig. 4*C* display the probability distribution functions for each question and for each rater before and after the workshop.

Table 2. *Questionnaire given to students before and after the workshop as well as evaluation method and criteria for question 2 ("What is the difference between an observation and an interpretation? Give an example.")*

Item	Example of Good Answers	Score
1. Observation	Description, analysis of a result, an image, by eye or under the microscope, what we see	1
2. Interpretation	Deduction, explanation	1
3. Difference	Interpretation first needs to observe since it is a possible explanation of a result; interpretation but not observation can be used to develop concepts, general rules	1
Example	A good example contained an observation and an interpretation	1

Table 3. *Questionnaire given to students before and after the workshop as well as evaluation method and criteria for question 3 ("What is the difference between a question and a hypothesis? Give an example.")*

Item	Example of Good Answers	Score
1. Question	A problem to solve	1
2. Hypothesis	A possible answer	1
3. Difference	To propose a hypothesis, one first needs to observe and to ask a question based on this observation	1
Example	A good example contained a question and a hypothesis	1

Posters. Before students took their posters back to school, we photographed them for a blind evaluation. This evaluation was performed by a researcher who had not participated to the workshop. We analyzed whether the title corresponded to the question students tested, the introduction explained the problem students were trying to solve, the general conclusion included a summary of all the results students obtained, the schematic drawing summarized the workshop, and links between the experiments performed by the three groups were clearly explained (see scoring shown in Table 5). More particularly, students were expected to understand how the results from the "fundamental research" groups (*groups 1* and *2*) could be used to develop a therapeutic strategy, based on the work conducted by the more "applied research" group (*group 3*). We also expected students to understand how the recombinant insulin produced by *group 3* could be tested using models established by *group 1*, which dose of insulin and route of administration should be used for the treatment with recombinant insulin, and how the dynamic and dose-dependent responses of pancreatic cells demonstrated by *group 2* would inform these decisions. To do so, we explained during the experimental session the possible consequences of inadequate doses of insulin on the efficacy or toxicity of the treatment since high doses might be lethal (not enough circulating glucose for brain function) and small doses might be inefficient. We also explained the different possible routes of administration. We looked for the presence of an explanation

Table 4. *Questionnaire given to students before and after the workshop as well as evaluation method and criteria for question 4 ("How do you make sure that the result obtained from an experiment is a valid result?"*

Item	Good Answers	Score
1	The repetition of each experiment many times	1
2	The use of control experiments	1

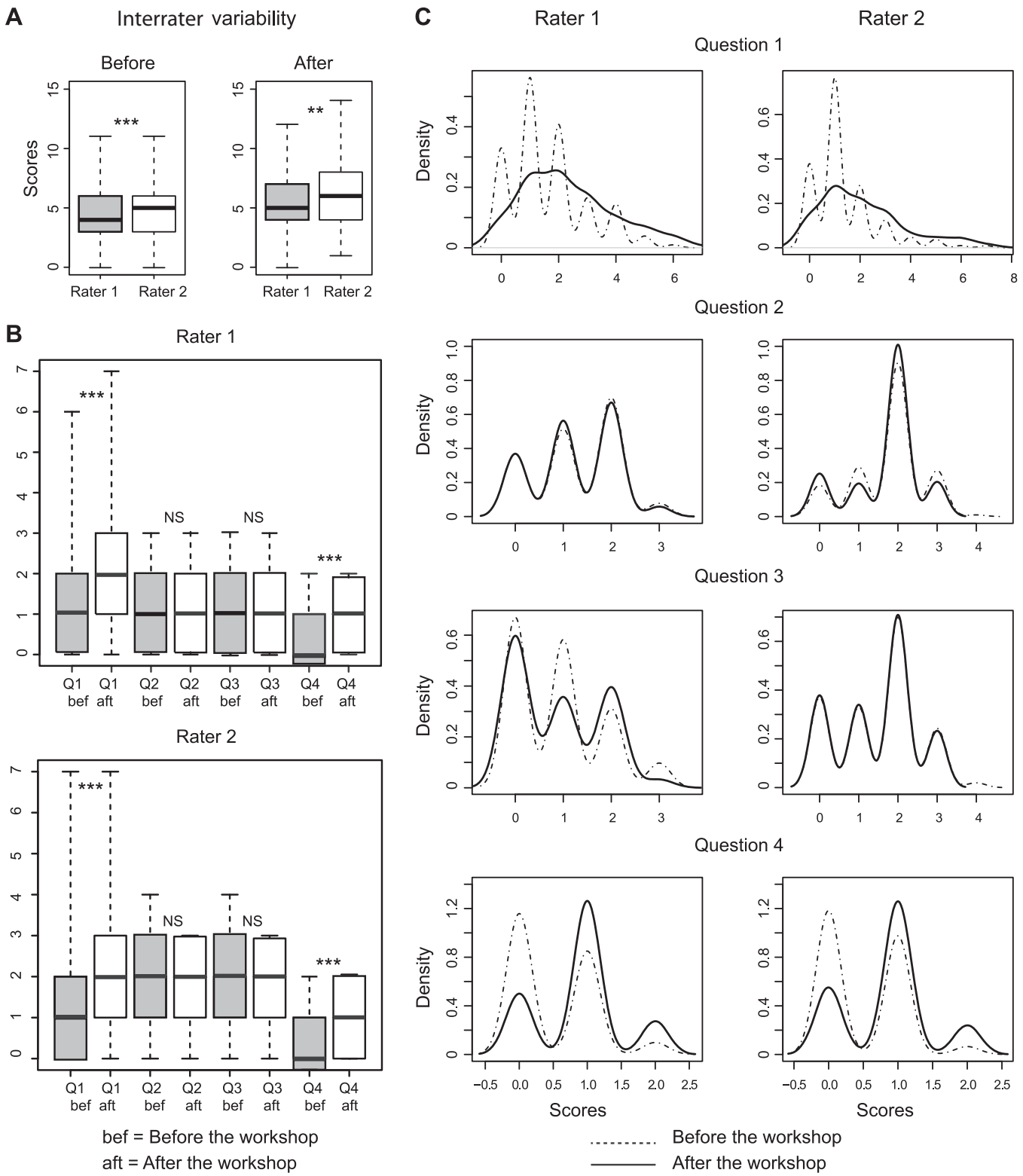

Fig. 4. Interrater variability and distribution of questionnaire scores before and after the workshop. *A*: interrater variability is shown as boxplots of the scores summed over all questions given by *rater 1* (shaded boxes) versus *rater 2* (open boxes) before (*left*) and after (*right*) the workshop. ***$P < 0.001$; **$P < 0.01$ (by Wilcoxon test). In the boxplots, the thick horizontal line is the median score, the *top* and *bottom* are the interquartile distance, and whiskers extend to data extremes. *B*: student scores for each question [*questions 1–4* (Q1–Q4)] before (bef) and after (aft) the workshop given by *rater 1* (*top*) or *rater 2* (*bottom*). NS, not signficant. ***$P < 0.001$ (by paired *t*-test). *C*: density plots showing the distribution of the scores given by *rater 1* (*left*) and *rater 2* (*right*) for each of the four questions before (dashed-dotted line) and after (solid line) the workshop. Each distribution reflects the frequency of individuals who obtained each of the possible scores for the corresponding question. Scores were determined using the evaluation criteria shown in Tables 1–4.

Table 5. *Evaluation method used to analyze the posters produced by students at the end of the workshop*

Item	Expected Elements	Score
1. Title	A sentence, preferably a question, summarizing the theme of the workshop.	5
2. Introduction	A short description of the scope and aims of the experimentation.	5
3. Conclusion	Schematic drawing summarizing the workshop.	10
4. Links	Links between *experiments 1–3* logically connecting the conclusions of each group.	15

of this link in the poster (Table 5). Altogether, 49 posters were produced.

RESULTS

Seventeen classes took part in this "diabetes workshop" between 2008 and 2013 comprising 420 students ranging in age from 15 to 17 yr, in the 11th grade, with a sex ratio of 55% male students and 45% female students.

Open-Ended Questioning (Phase 1)

When discussing the etiology of diabetes, students often suggested that the number of diabetic people in a country varied as a function of what they ate, how much they exercised, and their genetic background. During the workshop, they realized that alloxan-treated diabetic mice had a reduced number of pancreatic β-cells (15), which helped them understand the etiology of the disease and that the destruction of pancreatic β-cells might be the cause of the loss of glycemia regulation. We explained at the end of the workshop the autoimmune cause of type I diabetes and the differences between various types of diabetes. On the question of how to study an illness and find medications to treat it, a high proportion of the students mentioned that they would have to test any medication before using it on humans. They often suggested doing in vitro experiments or using animal models of the disease to understand the illness and test therapeutic strategies. The discussion often focused on the advantages and limitations of various kinds of experimental models (animal vs. cellular models) depending on the nature of the question (ranging from general glucose physiology questions to the function of the pancreatic cells or the evaluation of potential treatments). To better understand the function of the pancreas and pancreatic cells, they often proposed taking out the pancreas from animal models, giving animals a glucose-rich diet, or injecting animals with a virus (to test whether a viral infection could destroy pancreatic β-cells). Regarding the design of a therapeutic strategy, most students suggested injecting insulin, grafting a pancreas, or using stem cells to replace damaged pancreatic cells. Representative results obtained by the students following laboratory protocols are described in Ref. 15.

Evaluation of Student Work

Questionnaire. Wilcoxon tests showed that scores before and after the session differed significantly between the two evaluators ($P < 0.001$; Fig. 4*A*). This was not unexpected as different raters often have different rating ranges and thresholds, even when provided with an evaluation grid. Most importantly, scores were significantly higher after the workshop than before for both raters for *questions 1* and *4* ($P < 0.001$ by a paired *t*-test), thus indicating a significant impact of the workshop on student responses. Scores were, however, not significantly different before and after the workshop for *questions 2* and *3* ($P = 0.7$ or 0.8 for *question 2* and $P = 0.5$ or 0.7 for *question 3* by a paired *t*-test; Fig. 4*B*). Density plots of the total scores for each question and for each rater also confirmed that the workshop changed the score distribution for *questions 1* and *4* only (Fig. 4*C*). For *question 1*, it shifted the distribution to the right (toward higher scores); for *question 4*, it increased the number of good answers for both *items 1* and *2* (see Tables 1–4 for the definition of items). The workshop improved the average score for *questions 1* and *4* for about 50% of the students (51% and 40%, respectively) and to *questions 2* and *3* for about 25% of the students (25% and 26%, respectively). The nonimprovement was not due to the fact that answers were already good before, since maximal scores were never observed before the workshop for *questions 1–3* and were observed for only 2.5% of the students for *question 4*.

For *question 1*, 39% of the students answered preworkshop that a researcher performs experiments to improve people's lives or to identify new medicine, treatments, or technologies. That fundamental research aims at increasing scientific knowledge was mentioned by 18% of the students preworkshop. After the workshop, students did not focus as much on either of these items, since the corresponding percentages dropped to 20% and 11%. In contrast, the scientific method used by researchers during their daily job, mentioned preworkshop by only 15%, doubled to 30% after the workshop. Despite this significant increase, the description of the scientific approach was often stereotyped and linear: "observation, questioning, hypothesis, experimentation, interpretation, conclusion and communication." The iterative aspects of the research process (requiring a permanent reevaluation of the hypotheses/models in the light of new results) were very rarely discussed, even though most of the students had to face this situation at least once during the workshop (i.e., obtaining a different result from the result a priori expected or obtaining a noninterpretable result).

Few students provided examples when answering *question 2* either before or after the workshop (5%), but the examples given after the workshop were more precise and relevant to scientific topics. In most cases, students did not understand the requirement for objective measurements to define an observation as opposed to the subjective nature of interpretation.

For *question 3*, 50% of the students knew that a hypothesis is a possible answer to a question, which needs to be tested by experimentation, and this was not changed by the workshop (51%). Preworkshop, only 27% of the students knew that a question is a problem derived from an observation and that one wants to solve. This increased slightly to 34% after the workshop. Few students provided examples when answering *question 3* either before or after the workshop (8%), but, as for *question 2*, the examples given after the workshop were more precise and relevant to scientific topics. To avoid this problem, we have now changed *questions 2* and *3* to "Give an example that illustrates the difference between an observation and an interpretation" and "Give an example that illustrates the difference between a question and a hypothesis."

In their answers to *question 4*, preworkshop only 14% of the students intended to include controls in their experiments, but

this almost quadrupled after the workshop (51%). Thirty-five percent of the students also knew preworkshop that an experiment needs to be repeated several times to make valid conclusions, and this did not change significantly after the workshop (37%). This is likely due to the emphasis put on the importance of experimental controls during the workshop and to constraints on time that ruled out multiple iterations of each experiment during the workshop.

Posters. Among the 49 posters, 60% met *criteria 1–3* and 50% met *criterion 4* (Table 5). This means that 40% had difficulty understanding the experiments of other groups and linking the results obtained by the three groups in the time allocated. To further improve this result, we decided to increase the discussion time with each group before the poster session. To allow students to collectively discuss and better understand all the results presented by the three groups, we also asked teachers to engage the whole class in a general discussion aimed at synthesizing results during the 2 wk after the workshop.

In conclusion, the evaluation of the questionnaires and posters indicated that this workshop successfully improved student awareness and understanding of the scientific reasoning and research process.

DISCUSSION

The objectives of the workshop were to help students understand how the scientific facts and results they learn in biology courses are generated in research laboratories and how fundamental research relates to therapeutic innovations via hands-on experiments on the regulation of glycemia and type I diabetes in a multidisciplinary context. The main idea was to recapitulate the different stages of the scientific research process in 3 days: observation of previous results, generation of hypotheses, experimentation, discussion, and communication of the results obtained. During the first morning of the workshop, the learning method relied on open inquiry since students generated scientific questions and proposed experimental strategies to test their hypotheses. During the experimentation phase of the workshop (afternoon of *day 1* and mornings of *days 2* and *3*; see Ref. 15), the educational method was based on facilitated inquiry since the teaching team provided guidelines for experimental design and methodological approaches.

Active learning via hands-on experiments was recently demonstrated to be more effective than more passive traditional lecturing, especially for the many high school students that experience difficulty with abstraction (5). The workshop presented in this article further supports this conclusion as we observed that both open-ended inquiry (during *phase 1* of the workshop) and facilitated inquiry (during *phase 2* of the workshop) facilitated the learning process. As demonstrated by the improvement of the student answers to *questions 1* and *4* after the workshop, this teaching approach promoted a good understanding of the methods associated with scientific research and, more generally, of the step-wise intellectual process required to draw valid and rigorous conclusions (observation, hypothesis generation, experimentation, notion of reproducibility and controls, and interpretation). In our opinion, this result is one of the main benefits of this educational approach. The improvement in student understanding of the scientific method and rigorous reasoning will not only be helpful to those students who will later start a scientific career but will also help all students to form rational and logical thoughts and opinions.

One possible explanation for the success of the approach is that it stimulates student's critical thinking compared with traditional teaching settings, which favor passive acquisition of established facts. Another possible explanation is that experimentation led students to make errors, which prompted them to stop their activities and take the time to think about their method, results, and the scientific question. Overall, experimentation and its associated results whether they were positive or negative systematically stimulated further questioning and thus promoted a deeper understanding of the biological question and facilitated the memorization of the acquired knowledge.

The success of the approach is exemplified by the fact that 60% of the posters satisfied *criterion 3*, indicating that the students had a good understanding of the learning topic and the experiments performed by the different groups by the end of the workshop. Importantly, that 50% of the posters also met the *criterion 4* showed that students developed good critical thinking skills as they were able to logically connect the work from each group and develop a full understanding of the workshop, glycemia regulation, and how to manipulate it to develop therapeutics. Finally, students often reported that having 3 full days dedicated to the same subject without interruption by other courses allowed them to gain a more comprehensive understanding of the topic.

This workshop also has some limitations, as evidenced by the fact that not all answers from the questionnaire improved after the workshop. Notions such as observations, interpretations, questions, and hypotheses are difficult for the students to conceptualize, and the workshop did not help most of them acquiring a better understanding of these notions. One possible explanation is that the emphasis of the workshop is really on the scientific method and analytic process (i.e., *questions 1* and *4* of the questionnaire), and, even though students generated observations, interpretations, questions, and hypotheses during the workshop, tutors did not ask students to identify and explicitly spell out these different elements of scientific reasoning. More attention should be dedicated to these concepts in future workshops. One strategy would be to ask students to identify the observation, question, hypothesis, and interpretation at each step of the open-ended and facilitated inquiry phases. This should allow students to become more familiar with these notions. Another limitation lies in the duration of the workshop (3 days), which is appropriate for most groups but too short for some other groups of students who needed more time to assimilate the new concepts and methodology of the workshop. Adding 1 more day to the workshop might thus be beneficial as it would allow some of the students to better finalize the PowerPoint presentation or poster.

This activity is suitable for high school students of the 11th and 12th grades as long as they have access to a well-equipped laboratory. It cannot be directly implemented in a classroom setting, given that it requires laboratory equipment not available in high schools. However, where the experiments cannot be performed, this educational approach can still be adapted for high school classrooms, by adopting the same learning method but using published documents (1, 11, 20, 21). On the other end, if given more time and in a university setting, undergrad-

uate students could be asked to fully design the experimental strategy and protocols so that the workshop becomes an entirely open-ended teaching experience. It is also possible to use the same framework for other topics in science. For example, Hippocampe maths laboratories in France (http://www.irem.univ-mrs.fr/-Hippocampe-.html) are a direct application of our framework to mathematics. This teaching format is also applicable to physics (we actually also propose a biology-physics workshop) and all experimental sciences in general.

The workshop results from extensive collaboration among researchers, doctoral and postdoctoral students, and high school science teachers. Doctoral students or postdoctoral fellows were trained for this innovative learning experience. This training was very beneficial for those who wanted to apply for university positions with teaching requirements. On the other hand, high school teachers reported that the workshop facilitated their teaching; it was a good introduction to their course on glycemia regulation and improved the cohesion of the class even weeks later. Finally, it took around 6 mo to design the present workshop. This kind of collaboration could definitely be initiated elsewhere, and we hope that the success of this workshop will motivate other research centers and/or universities to offer high school students the opportunity to conduct experimental science and inquiry-based learning. A university laboratory dedicated to hands-on experiments for high school students exists in a few research centers: in Israel, in Europe (for a review, see Ref. 8), and in the United States (e.g., the community lab at Biogen, Cambridge, MA; https://www.biogen.com/en_us/responsibility/community-lab.html).

ACKNOWLEDGMENTS

The authors thank Tamara Ben Ari for help with the questionnaire and statistical analyses and Jaime Darce for discussion and critical review of this manuscript. The freely available R program was used for statistical analyses (**R Core Team**. *R: a Language and Environment for Statistical Computing*. Vienna: R Foundation for Statistical Computing, 2014).

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GRANTS

Tous Chercheurs is supported by the Institut National de la Santé et de la Recherche Médicale, Ministère de l'Education Nationale, de l'Enseignement Supérieur et de la Recherche, Région Provence-Alpes-Côte d'Azur, Direction Régionale de la Recherche et de la Technologie, Aix-Marseille Université, Ville de Marseille, and Haut Commissariat à la Jeunesse, France.

DISCLOSURES

No conflicts of interest, financial or otherwise, are declared by the author(s).

AUTHOR CONTRIBUTIONS

Author contributions: M.M., A.C., N.S., J.C., A.R., C.H., and J.T. conception and design of research; M.M., A.C., N.S., J.C., A.R., C.H., and J.T. performed experiments; M.M., A.C., N.S., J.C., A.R., C.H., and J.T. analyzed data; M.M., A.C., N.S., J.C., A.R., C.H., and J.T. interpreted results of experiments; M.M., C.H., and J.T. prepared figures; M.M., C.H., and J.T. drafted manuscript; M.M., C.H., and J.T. edited and revised manuscript; M.M. approved final version of manuscript.

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